

REMARKS

Upon entry of the Amendment, claims 14 to 27, 29 to 30, and 43 to 66 are pending in the application. The specification is amended. Claims 1 to 13, 28, and 31 to 42 are canceled. Claims 14 to 27 are withdrawn from consideration. Claims 14 to 17, 21 to 27, and 29 to 30 are amended. Claims 43 to 66 are new.

No new matter is added. Withdrawn claim 14 is amended for the purpose of a possible rejoinder thereof. Withdrawn claims 15 and 16 are amended, in view of the amendment to withdrawn claim 14. Withdrawn claims 21 to 27 are amended in view of the cancellation of claims 1 to 13. The specification supports the amendments to claims 29 and 30, such as on pages 7 to 9. The specification supports new claims 43 to 66, such as on pages 7 to 9. Entry of the amendment is respectfully requested.

I. Election/Restriction

Referring to pages 2 to 3 of the Office Action, the Examiner asserts that Groups XXXI, X, XI, and XII do not share the same technical feature.

Applicants respectfully submit that the examination of Groups XXXI, X, XI, and XII would not result in an unduly burdensome search. Example 4 of the present specification discloses that each of SEQ ID NO: 4, SEQ ID NO: 7, and SEQ ID NO: 10 differ from the amino acid sequence of SEQ ID NO: 1 by one amino acid.

II. Specification

The specification is objected to allegedly because of the use of improperly demarcated trademarks.

The specification is amended in an effort to refer to trademarks.

III. Claim Rejections - 35 U.S.C. § 112

(A) Claims 29 and 30 are rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite.

The Examiner asserts that the phrase “the same or substantially is indefinite the same amino acid sequence as the amino acid sequence represented by SEQ ID NO: 1.”

Claims 29 and 30 are amended. Applicants respectfully submit that a person skilled in the art can understand the metes and bounds of claims 29 and 30, as presently recited.

(B) Claims 29 to 30 are rejected under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the written description requirement.

The Examiner asserts that the specification fails to provide written description support for a protein having “substantially the same” amino acid sequence as the amino acid sequence of SEQ ID NO: 1 or the claimed partial peptide. The Examiner asserts that a person skilled in the art could not immediately envision, recognize or distinguish most of the members of the genus.

Applicants respectfully submit that the specification provides written description support to amended claims 29 and 30. Page 9 of the specification describes that the protein may have 1 to 10 substitutions, deletions, or insertions. Example 8 of the specification also describes producing antibodies with peptides having the amino acid sequence present at position 402 to 412 of SEQ ID NO: 1, 582 to 596 of SEQ ID NO: 1, 781 to 794 of SEQ ID NO: 1, and 797 to 809 of SEQ ID NO: 1. *See Example 8 of the Specification.* Further, the specification provides the amino acid sequences of SEQ ID NOS: 4, 7, and 10. SEQ ID NO: 4 differs from SEQ ID NO: 1 at position 208. SEQ ID NO: 7 differs from SEQ ID NO: 1 at position 163. SEQ ID NO: 10 differs from SEQ ID NO: 1 at position 364.

In view of the above descriptions, a person skilled in the art can predict the amino acid sequence of an amino acid sequence in which 1 to 10 amino acid sequences have been substituted, deleted or inserted into SEQ ID NO: 1, wherein said substitution, deletion, or insertion is with an amino acid position outside of position 402 to 412 of SEQ ID NO: 1, 582 to 596 of SEQ ID NO: 1, 781 to 794 of SEQ ID NO: 1, and 797 to 809 of SEQ ID NO: 1. The amino acid sequence indicates which positions may include the substitution, deletion, or insertions of 1 to 10 amino acids. Example 8 describes using peptides having the amino acids at positions 402 to 412, 582 to 596, 781 to 794, and 797 to 809 of SEQ ID NO: 1 to produce the antibodies thereof. The specification provides examples of such an amino acid sequence in SEQ ID NOs: 4, 7, and 10. In this regard, the specification provides written description support to amended claims 29 and 30.

IV. Claim Rejections - 35 U.S.C. § 102

The Office Action contains two rejections under 35 U.S.C. § 102, as follows:

claims 29 to 30 are rejected under 35 U.S.C. § 102(b) as allegedly being anticipate by Osada et al.; and

claims 29 and 30 are rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Cuello et al.

With respect to Osada, the Examiner asserts that Osada discloses an antiphosphotyrosine monoclonal antibody that specifically binds to phosphotyrosine amino acids. The Examiner asserts that SEQ ID NO: 1 includes multiple tyrosine residues.

Applicants respectfully submit that Osada fails to describe or suggest an antibody that specifically binds to the claimed proteins. Figure 2 of Osada indicates that the antiphosphotyrosine antibody thereof unspecifically binds to proteins including phosphotyrosine amino acids. In this regard, Figure 2 of Osada indicates that the antiphosphotyrosine antibody

thereof may bind to proteins that do not comprise the amino acid sequence of SEQ ID NO: 1 or to proteins in which one to ten amino acids have deleted from, inserted into, or substituted into the amino acid sequence of SEQ ID NO: 1, wherein said deletion, insertion, or substitution occurs at an amino acid position outside of positions 402 to 412 of SEQ ID NO: 1, 582 to 596 of SEQ ID NO: 1, 781 to 794 of SEQ ID NO: 1, and 797 to 809 of SEQ ID NO: 1. More than a phosphotyrosine amino acid, if any, is present at positions 402 to 412, 582 to 596, 781 to 794, and 797 to 809 of SEQ ID NO: 1. In this regard, the antiphosphotyrosine antibody is not specific to the proteins recited in claims 29 and 30.

With respect to Cuello, the Examiner asserts that Cuello describes an antibody that binds to an erbB-2 polypeptide (i.e., trastuzumab). The Examiner asserts that the protein recited in claims 29 and 30 would encompass erbB-2 as disclosed in Cuello.

Applicants Cuello fails to expressly describe the amino acid sequence of the erbB-2 polypeptide thereof. Cuello discloses using erbB-2 from several cell lines (SKBr-3, MDA-MB-453, SKOv-3, MDA-MB-468, SW-626, MDA-MB-231, and MCF-7). *See* Cuello, p. 4892-4893. GENBANK™ provides the amino acid sequence of Receptor tyrosine-protein kinase erbB-2 precursor (p185erbB2). A copy of the amino acid sequence is provided herewith. Based on a comparison with the Receptor tyrosine-protein kinase erbB-2, it appears that amino acid sequences of the claimed proteins are significantly different. In this regard, the antibody disclosed in Cuello is different from the antibody recited in claims 29 and 30.

V. Double Patenting

Claims 29-30 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting, as allegedly being unpatentable over claims 1-14 of copending Application no. 10/584,183.

Applicants defer responding at this time to this provisional obviousness-type double patenting rejection, pursuant to MPEP § 804(I)(B).

In view of the above, reconsideration and allowance of this application are now believed to be in order, and such actions are hereby solicited. If any points remain in issue which the Examiner feels may be best resolved through a personal or telephone interview, the Examiner is kindly requested to contact the undersigned at the telephone number listed below.

The USPTO is directed and authorized to charge all required fees, except for the Issue Fee and the Publication Fee, to Deposit Account No. 19-4880. Please also credit any overpayments to said Deposit Account.

Respectfully submitted,


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Features: CDD

1: P04626. Reports Receptor tyrosine...[gi:119533]

BLINK, Conserved Domains, Links

Comment Features Sequence

LOCUS P04626 1255 aa linear PRI 10-JUL-2007

DEFINITION Receptor tyrosine-protein kinase erbB-2 precursor (p185erbB2) (C-erbB-2) (NEU proto-oncogene) (Tyrosine kinase-type cell surface receptor HER2) (MLN 19) (CD340 antigen).

ACCESSION P04626

VERSION P04626 GI:119533

DBSOURCE swissprot: locus ERBB2_HUMAN, accession P04626; class: standard. extra accessions: Q14256, Q6LDV1, Q9UMK4 created: Aug 13, 1987. sequence updated: Aug 13, 1987. annotation updated: Jul 10, 2007.

xrefs: M11767_1, AAA35808_1, M11761_1, M11762_1, M11763_1, M11764_1, M11765_1, M11766_1, M11730_1, AAA75493_1, M12036_1, AAA35978_1, AY208911_1, AAO18082_1, X03363_1, CAA27060_1, M16792_1, AAA58637_1, M16789_1, M16790_1, M16791_1, L29395_1, AAA35809_1, M95667_1, AAC37531_1, A24571, IN8ZC_1, I0VC_A, IQR1F, I178A, I178B, 2A91A

xrefs (non-sequence databases): UniGene:Hs.446352, DIP:DIP:8N, IntAct:P04626, Ensembl:ENSG00000141736, KEGG:hsa:2064, HGNC:3430, HPA:CA000043, HPA:HPA001383, MIM: 164870, PharmGKB:PA27844, DrugBank:BD00098, LinkHub:P04626, ArrayExpress:P04626, GermOnline:ENSG00000141736, RZPD-ProtExp:B0017, GO:0016021, GO:0005886, GO:0005006, GO:0043125, GO:0042802, GO:0046982, GO:0004716, GO:0007507, GO:0030879, GO:0007399, GO:0048015, GO:0050679, GO:0043406, GO:0006468, GO:0045765, GO:0007169, InterPro:IPR000494, InterPro:IPR006211, InterPro:IPR006212, InterPro:IPR000719, InterPro:IPR001245, InterPro:IPR008266, InterPro:IPR004019, Pfam:PF00757, Pfam:PF07714, Pfam:PF01030, Pfam:PF02757, PRINTS:PRO0109, ProDom:PD000001, SMART:SM00261, SMART:SM00219, PROSITE:PS00107, PROSITE:PS50011, PROSITE:PS00109

KEYWORDS 3D-structure; ATP-binding; Glycoprotein; Kinase; Membrane; Nucleotide-binding; Phosphorylation; Polymorphism; Receptor; Signal; Transferase; Transmembrane; Tyrosine-protein kinase.

SOURCE Homo sapiens (human)

ORGANISM Homo sapiens

Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi; Mammalia; Eutheria; Euarchontoglires; Primates; Haplorrhini; Catarrhini; Hominoidea; Homo.

REFERENCE 1 (residues 1 to 1255)

AUTHORS Yamamoto, T., Ikawa, S., Akiyama, T., Semba, K., Nomura, N., Miyajima, N., Saito, T. and Toyoshima, K.

TITLE Similarity of protein encoded by the human c-erb-B-2 gene to epidermal growth factor receptor

JOURNAL Nature 319 (6050), 230-234 (1986)

PUBMED 3003577

REMARK NUCLEOTIDE SEQUENCE [mRNA].
 REFERENCE 2 (residues 1 to 1255)
 AUTHORS Coussens,L., Yang-Feng,T.L., Liao,Y.C., Chen,E., Gray,A., McGrath,J., Seeburg,P.H., Libermann,T.A., Schlessinger,J., Francke,U., Levinson,A. and Ullrich,A.
 TITLE Tyrosine kinase receptor with extensive homology to EGF receptor shares chromosomal location with neu oncogene
 JOURNAL Science 230 (4730), 1132-1139 (1985)
 PUBMED 2999974
 REMARK NUCLEOTIDE SEQUENCE [GENOMIC DNA / mRNA], AND VARIANT ALA-1170.
 REFERENCE 3 (residues 1 to 1255)
 AUTHORS Rieder,M.J., Livingston,R.J., Daniels,M.R., Montoya,M.A., Chung,M.-W., Miyamoto,K.B., Nguyen,C.P., Nguyen,D.A., Poel,C.L., Robertson,P.D., Schackwitz,W.S., Sherwood,J.K., Witruk,L.A. and Nickerson,D.A.
 TITLE Direct Submission
 JOURNAL Submitted (??-DEC-2002)
 REMARK NUCLEOTIDE SEQUENCE [GENOMIC DNA], AND VARIANTS CYS-452; VAL-655 AND ALA-1170.
 REFERENCE 4 (residues 1 to 1255)
 AUTHORS Tal,M., King,C.R., Kraus,M.H., Ullrich,A., Schlessinger,J. and Givol,D.
 TITLE Human HER2 (neu) promoter: evidence for multiple mechanisms for transcriptional initiation
 JOURNAL Mol. Cell. Biol. 7 (7), 2597-2601 (1987)
 PUBMED 3039351
 REMARK NUCLEOTIDE SEQUENCE [GENOMIC DNA] OF 1-191.
 REFERENCE 5 (residues 1 to 1255)
 AUTHORS Semba,K., Kamata,N., Toyoshima,K. and Yamamoto,T.
 TITLE A v-erbB-related protooncogene, c-erbB-2, is distinct from the c-erbB-1/epidermal growth factor-receptor gene and is amplified in a human salivary gland adenocarcinoma
 JOURNAL Proc. Natl. Acad. Sci. U.S.A. 82 (19), 6497-6501 (1985)
 PUBMED 2995967
 REMARK NUCLEOTIDE SEQUENCE [GENOMIC DNA] OF 737-1031.
 REFERENCE 6 (residues 1 to 1255)
 AUTHORS King,C.R., Kraus,M.H. and Aaronson,S.A.
 TITLE Amplification of a novel v-erbB-related gene in a human mammary carcinoma
 JOURNAL Science 229 (4717), 974-976 (1985)
 PUBMED 2992089
 REMARK NUCLEOTIDE SEQUENCE OF 832-909.
 TISSUE=Mammary carcinoma
 REFERENCE 7 (residues 1 to 1255)
 AUTHORS Sarkar,F.H., Ball,D.E., Li,Y.W. and Crissman,J.D.
 TITLE Molecular cloning and sequencing of an intron of Her-2/neu (ERBB2) gene
 JOURNAL DNA Cell Biol. 12 (7), 611-615 (1993)
 PUBMED 8104414
 REMARK NUCLEOTIDE SEQUENCE OF 1081-1245, AND VARIANT ALA-1170.
 REFERENCE 8 (residues 1 to 1255)
 AUTHORS Arcaro,A., Zvelebil,M.J., Wallasch,C., Ullrich,A., Waterfield,M.D. and Domin,J.
 TITLE Class II phosphoinositide 3-kinases are downstream targets of activated polypeptide growth factor receptors
 JOURNAL Mol. Cell. Biol. 20 (11), 3817-3830 (2000)
 PUBMED 10805725
 REMARK IDENTIFICATION IN A COMPLEX WITH PIK3C2A AND EGFR, IDENTIFICATION IN A COMPLEX WITH PIK3C2B AND EGFR, AND INTERACTION WITH PIK3C2B.
 REFERENCE 9 (residues 1 to 1255)
 AUTHORS Swiercz,J.M., Kuner,R. and Offermanns,S.
 TITLE Plexin-B1/RhoGEP-mediated RhoA activation involves the receptor tyrosine kinase Erbb-2
 JOURNAL J. Cell Biol. 165 (6), 869-880 (2004)

PUBMED 15210733
REMARK INTERACTION WITH PLXNB1.
REFERENCE 10 (residues 1 to 1255)
AUTHORS Marone,R., Hess,D., Dankort,D., Muller,W.J., Hynes,N.E. and Badache,A.
TITLE Memo mediates ErbB2-driven cell motility
JOURNAL Nat. Cell Biol. 6 (6), 515-522 (2004)
PUBMED 15156151
REMARK INTERACTION WITH MEMO.
REFERENCE 11 (residues 1 to 1255)
AUTHORS Olsen,J.V., Blagoev,B., Gnad,F., Macek,B., Kumar,C., Mortensen,P. and Mann,M.
TITLE Global, in vivo, and site-specific phosphorylation dynamics in signaling networks
JOURNAL Cell 127 (3), 635-648 (2006)
PUBMED 17081983
REMARK PHOSPHORYLATION [LARGE SCALE ANALYSIS] AT TYR-1248, AND MASS SPECTROMETRY.
TISSUE=Epithelium
REFERENCE 12 (residues 1 to 1255)
AUTHORS Kuhns,J.J., Batalia,M.A., Yan,S. and Collins,E.J.
TITLE Poor binding of a HER-2/neu epitope (GP2) to HLA-A2.1 is due to a lack of interactions with the center of the peptide
JOURNAL J. Biol. Chem. 274 (51), 36422-36427 (1999)
PUBMED 10593938
REMARK X-RAY CRYSTALLOGRAPHY (2.4 ANGSTROMS) OF 654-662 IN COMPLEX WITH HLA AND BETA-2 MICROGLOBULIN.
REFERENCE 13 (residues 1 to 1255)
AUTHORS Cho,H.S., Mason,K., Ramyar,K.X., Stanley,A.M., Gabelli,S.B., Denney,D.W. Jr. and Leahy,D.J.
TITLE Structure of the extracellular region of HER2 alone and in complex with the Herceptin Fab
JOURNAL Nature 421 (6924), 756-760 (2003)
PUBMED 12610629
REMARK X-RAY CRYSTALLOGRAPHY (2.52 ANGSTROMS) OF 23-629 IN COMPLEX WITH FAB.
REFERENCE 14 (residues 1 to 1255)
AUTHORS Ehsani,A., Low,J., Wallace,R.B. and Wu,A.M.
TITLE Characterization of a new allele of the human ERBB2 gene by allele-specific competition hybridization
JOURNAL Genomics 15 (2), 426-429 (1993)
PUBMED 8095488
REMARK VARIANTS VAL-654 AND VAL-655.
COMMENT On Mar 15, 2005 this sequence version replaced gi:86984.
[FUNCTION] Essential component of a neuregulin-receptor complex, although neuregulins do not interact with it alone. GP30 is a potential ligand for this receptor. Not activated by EGF, TGF-alpha and amphiregulin.
[CATALYTIC ACTIVITY] ATP + a [protein]-L-tyrosine = ADP + a [protein]-L-tyrosine phosphate.
[SUBUNIT] Heterodimer with each of the other ERBB receptors (Potential). Interacts with PRKCABP and PLXNB1. Part of a complex with EGFR and either PIK3C2A or PIK3C2B. May interact with PIK3C2B when phosphorylated on Tyr-1196. Interacts with MEMO when phosphorylated on Tyr-1248.
[INTERACTION] Self; NbExp=1; IntAct=EBI-641062, EBI-641062; P62157:CALM (xeno); NbExp=1; IntAct=EBI-641062, EBI-397403; P62161:Calml (xeno); NbExp=1; IntAct=EBI-641062, EBI-397530; P00533:EGFR; NbExp=2; IntAct=EBI-641062, EBI-297353; P21860:ERBB3; NbExp=4; IntAct=EBI-641062, EBI-720706; Q15303:ERBB4; NbExp=2; IntAct=EBI-641062, EBI-80371.
[SUBCELLULAR LOCATION] Membrane; Single-pass type I membrane protein.
[PTM] Ligand-binding increases phosphorylation on tyrosine residues

(By similarity).

[POLYMORPHISM] There are four alleles due to the variations in positions 654 and 655. Allele B1 (Ile-654/Ile-655) has a frequency of 0.782; allele B2 (Ile-654/Val-655) has a frequency of 0.206; allele B3 (Val-654/Val-655) has a frequency of 0.012.

[SIMILARITY] Belongs to the Tyr protein kinase family. EGF receptor subfamily.

[SIMILARITY] Contains 1 protein kinase domain.

[WEB RESOURCE] NAME=Atlas of Genetics and Cytogenetics in Oncology and Haematology;

URL='<http://atlasgeneticsoncology.org/Genes/ERBB2ID162ch17q11.html>'.

[WEB RESOURCE] NAME=Wikipedia ERBB2 entry;

URL='<http://en.wikipedia.org/wiki/ERBB2>'.

FEATURES

	Location/Qualifiers
source	1..1255 /organism="Homo sapiens" /db_xref="taxon:9606"
gene	1..1255 /gene="ERBB2" /note="synonyms: HER2, NEU, NGL"
Protein	1..1255 /gene="ERBB2" /product="Receptor tyrosine-protein kinase erbB-2 precursor" /EC_number="2.7.10.1"
Region	1..22 /gene="ERBB2" /region_name="Signal" /inference="non-experimental evidence, no additional details recorded" /note="Potential."
Region	23..1255 /gene="ERBB2" /region_name="Mature chain" /experiment="experimental evidence, no additional details recorded" /note="Receptor tyrosine-protein kinase erbB-2. /FTId=PRO_0000016669."
Region	23..652 /gene="ERBB2" /region_name="Topological domain" /inference="non-experimental evidence, no additional details recorded" /note="Extracellular (Potential)."
Region	25..27 /gene="ERBB2" /region_name="Beta-strand region" /experiment="experimental evidence, no additional details recorded"
Region	39..50 /gene="ERBB2" /region_name="Helical region" /experiment="experimental evidence, no additional details recorded"
Region	52..173 /gene="ERBB2" /region_name="Recep_L_domain" /note="Receptor L domain. The L domains from these receptors make up the bilobal ligand binding site. Each L domain consists of a single-stranded right hand beta-helix. This Pfam entry is missing the first 50 amino acid residues of the domain; pfam01030" /db_xref="CDD:79745"

Region 55..64
/gene="ERBB2"
/region_name="Beta-strand region"
/experiment="experimental evidence, no additional details recorded"
Site 68
/gene="ERBB2"
/site_type="glycosylation"
/inference="non-experimental evidence, no additional details recorded"
/note="N-linked (GlcNAc...) (Potential)."
Region 72..74
/gene="ERBB2"
/region_name="Helical region"
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Region 79..82
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/experiment="experimental evidence, no additional details recorded"
Region 84..88
/gene="ERBB2"
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/experiment="experimental evidence, no additional details recorded"
Region 109..111
/gene="ERBB2"
/region_name="Hydrogen bonded turn"
/experiment="experimental evidence, no additional details recorded"
Region 112..117
/gene="ERBB2"
/region_name="Beta-strand region"
/experiment="experimental evidence, no additional details recorded"
Site 124
/gene="ERBB2"
/site_type="glycosylation"
/inference="non-experimental evidence, no additional details recorded"
/note="N-linked (GlcNAc...) (Potential)."
Region 152..157
/gene="ERBB2"
/region_name="Beta-strand region"
/experiment="experimental evidence, no additional details recorded"
Region 164..166
/gene="ERBB2"
/region_name="Hydrogen bonded turn"
/experiment="experimental evidence, no additional details recorded"
Region 169..172
/gene="ERBB2"
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/experiment="experimental evidence, no additional details recorded"
Region 175..177
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Region 182..184
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/region_name="Beta-strand region"
/experiment="experimental evidence, no additional details recorded"
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/gene="ERBB2"
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/inference="non-experimental evidence, no additional details recorded"
/note="N-linked (GlcNAc...) (Potential)."
Region 189..343
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/note="Furin-like cysteine rich region; pfam00757"
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/bond_type="disulfide"
/inference="non-experimental evidence, no additional details recorded"
/note="By similarity."
Bond bond(199,212)
/gene="ERBB2"
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/inference="non-experimental evidence, no additional details recorded"
/note="By similarity."
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/region_name="Beta-strand region"
/experiment="experimental evidence, no additional details recorded"
Region 204..208
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/experiment="experimental evidence, no additional details recorded"
Region 217..219
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/bond_type="disulfide"
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Region 232..234

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/experiment="experimental evidence, no additional details recorded"
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235..280
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/note="Furin-like repeats. Cysteine rich region. Exact function of the domain is not known. Furin is a serine-kinase dependent proprotein processor. Other members of this family include endoproteases and cell surface receptors; cd00064"
/db_xref="CDD:28946"
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bond(240,252)
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244..248
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/experiment="experimental evidence, no additional details recorded"
Region
251..260
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/experiment="experimental evidence, no additional details recorded"
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Site
259
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/inference="non-experimental evidence, no additional details recorded"
/note="N-linked (GlcNAc...) (Potential)."
Region
263..267
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/region_name="Beta-strand region"
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Bond
bond(268,295)
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/inference="non-experimental evidence, no additional details recorded"
Region
271..274

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recorded"
Region
276..278
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/region_name="Hydrogen bonded turn"
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recorded"
Region
281..283
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Region
289..291
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recorded"
Region
294..298
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Region
299..311
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Bond
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303..305
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/region_name="Beta-strand region"
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309..314
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/region_name="Beta-strand region"
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Bond
Region
315..331
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/inference="non-experimental evidence, no additional
details recorded"
/note="By similarity."
Region
319..323
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/region_name="Beta-strand region"
/experiment="experimental evidence, no additional details
recorded"
Region
329..333
/gene="ERBB2"
/region_name="Beta-strand region"
/experiment="experimental evidence, no additional details
recorded"
Bond
Region
334..338
/gene="ERBB2"
/bond_type="disulfide"
/inference="non-experimental evidence, no additional
details recorded"
/note="By similarity."
Region
335..337
/gene="ERBB2"
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/region_name="Beta-strand region"
/experiment="experimental evidence, no additional details recorded"
Region 348..350
/gene="ERBB2"
/region_name="Helical region"
/experiment="experimental evidence, no additional details recorded"
Region 358..360
/gene="ERBB2"
/region_name="Hydrogen bonded turn"
/experiment="experimental evidence, no additional details recorded"
Region 361..364
/gene="ERBB2"
/region_name="Helical region"
/experiment="experimental evidence, no additional details recorded"
Region 366..486
/gene="ERBB2"
/region_name="Recep_L_domain"
/note="Receptor L domain. The L domains from these receptors make up the bilobal ligand binding site. Each L domain consists of a single-stranded right hand beta-helix. This Pfam entry is missing the first 50 amino acid residues of the domain; pfam01030"
/db_xref="CDD:79745"
Region 368..376
/gene="ERBB2"
/region_name="Beta-strand region"
/experiment="experimental evidence, no additional details recorded"
Region 378..380
/gene="ERBB2"
/region_name="Helical region"
/experiment="experimental evidence, no additional details recorded"
Region 396..402
/gene="ERBB2"
/region_name="Helical region"
/experiment="experimental evidence, no additional details recorded"
Region 405..408
/gene="ERBB2"
/region_name="Beta-strand region"
/experiment="experimental evidence, no additional details recorded"
Region 410..413
/gene="ERBB2"
/region_name="Beta-strand region"
/experiment="experimental evidence, no additional details recorded"
Region 423..425
/gene="ERBB2"
/region_name="Helical region"
/experiment="experimental evidence, no additional details recorded"
Region 438..440
/gene="ERBB2"
/region_name="Hydrogen bonded turn"
/experiment="experimental evidence, no additional details recorded"
Region 441..447
/gene="ERBB2"

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/region_name="Beta-strand region"
/experiment="experimental evidence, no additional details
recorded"
Region
452
/gene="ERBB2"
/region_name="Variant"
/experiment="experimental evidence, no additional details
recorded"
/note="W -> C. /FTId=VAR_016317."
463..469
/gene="ERBB2"
/region_name="Beta-strand region"
/experiment="experimental evidence, no additional details
recorded"
Region
482..485
/gene="ERBB2"
/region_name="Helical region"
/experiment="experimental evidence, no additional details
recorded"
Region
493..498
/gene="ERBB2"
/region_name="Beta-strand region"
/experiment="experimental evidence, no additional details
recorded"
Region
501..506
/gene="ERBB2"
/region_name="Helical region"
/experiment="experimental evidence, no additional details
recorded"
Region
509..544
/gene="ERBB2"
/region_name="FU"
/note="Furin-like repeats; smart00261"
/db_xref="CDD:47590"
Bond
bond(511,520)
/gene="ERBB2"
/bond_type="disulfide"
/inference="non-experimental evidence, no additional
details recorded"
/note="By similarity."
bond(515,528)
/gene="ERBB2"
/bond_type="disulfide"
/inference="non-experimental evidence, no additional
details recorded"
/note="By similarity."
Region
516..518
/gene="ERBB2"
/region_name="Helical region"
/experiment="experimental evidence, no additional details
recorded"
Region
520..524
/gene="ERBB2"
/region_name="Beta-strand region"
/experiment="experimental evidence, no additional details
recorded"
Region
528..536
/gene="ERBB2"
/region_name="Beta-strand region"
/experiment="experimental evidence, no additional details
recorded"
Site
530
/gene="ERBB2"
/site_type="glycosylation"
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/inference="non-experimental evidence, no additional details recorded"
Bond bond(531,540)
/gene="ERBB2"
/bond_type="disulfide"
/inference="non-experimental evidence, no additional details recorded"
/note="By similarity."
Region 539..542
/gene="ERBB2"
/region_name="Beta-strand region"
/experiment="experimental evidence, no additional details recorded"
Bond bond(544,560)
/gene="ERBB2"
/bond_type="disulfide"
/inference="non-experimental evidence, no additional details recorded"
/note="By similarity."
Region 545..551
/gene="ERBB2"
/region_name="Beta-strand region"
/experiment="experimental evidence, no additional details recorded"
Region 553..556
/gene="ERBB2"
/region_name="Beta-strand region"
/experiment="experimental evidence, no additional details recorded"
Region 557..603
/gene="ERBB2"
/region_name="FU"
/note="Furin-like repeats; smart00261"
/db_xref="CDD:47590"
Region 559..562
/gene="ERBB2"
/region_name="Beta-strand region"
/experiment="experimental evidence, no additional details recorded"
Bond bond(563,576)
/gene="ERBB2"
/bond_type="disulfide"
/inference="non-experimental evidence, no additional details recorded"
/note="By similarity."
Bond bond(567,584)
/gene="ERBB2"
/bond_type="disulfide"
/inference="non-experimental evidence, no additional details recorded"
/note="By similarity."
Region 571..573
/gene="ERBB2"
/region_name="Beta-strand region"
/experiment="experimental evidence, no additional details recorded"
Site 571
/gene="ERBB2"
/site_type="glycosylation"
/inference="non-experimental evidence, no additional details recorded"
/note="N-linked (GlcNAc...) (Potential)."
Region 575..580

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/gene="ERBB2"
/region_name="Beta-strand region"
/experiment="experimental evidence, no additional details
recorded"
Region
583..592
/gene="ERBB2"
/region_name="Beta-strand region"
/experiment="experimental evidence, no additional details
recorded"
Bond
bond(587,596)
/gene="ERBB2"
/bond_type="disulfide"
/inference="non-experimental evidence, no additional
details recorded"
/note="By similarity."
Region
595..599
/gene="ERBB2"
/region_name="Beta-strand region"
/experiment="experimental evidence, no additional details
recorded"
Bond
bond(600,623)
/gene="ERBB2"
/bond_type="disulfide"
/inference="non-experimental evidence, no additional
details recorded"
/note="By similarity."
Region
615..617
/gene="ERBB2"
/region_name="Beta-strand region"
/experiment="experimental evidence, no additional details
recorded"
Region
621..625
/gene="ERBB2"
/region_name="Beta-strand region"
/experiment="experimental evidence, no additional details
recorded"
Bond
bond(626,634)
/gene="ERBB2"
/bond_type="disulfide"
/inference="non-experimental evidence, no additional
details recorded"
/note="By similarity."
Site
629
/gene="ERBB2"
/site_type="glycosylation"
/inference="non-experimental evidence, no additional
details recorded"
/note="N-linked (GlcNAc...) (Potential)."
Bond
bond(630,642)
/gene="ERBB2"
/bond_type="disulfide"
/inference="non-experimental evidence, no additional
details recorded"
/note="By similarity."
Region
653..675
/gene="ERBB2"
/region_name="Transmembrane region"
/inference="non-experimental evidence, no additional
details recorded"
/note="Potential."
Region
654
/gene="ERBB2"
/region_name="Variant"
/experiment="experimental evidence, no additional details
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recorded"
/note="I -> V (in allele B3; dbSNP:rs1801201).
/FTId=VAR_004077."
Region 655
/gene="ERBB2"
/region_name="Variant"
/experiment="experimental evidence, no additional details recorded"
/note="I -> V (in allele B2 and allele B3;
dbSNP:rs1801200). /FTId=VAR_004078."
Region 676..1255
/gene="ERBB2"
/region_name="Topological domain"
/inference="non-experimental evidence, no additional details recorded"
/note="Cyttoplasmic (Potential)."
Region 715..979
/gene="ERBB2"
/region_name="TyrKc"
/note="Tyrosine kinase, catalytic domain.
Phosphotransferases; tyrosine-specific kinase subfamily;
cd00192"
/db_xref="CDD:29154"
720..987
/gene="ERBB2"
/region_name="Domain"
/experiment="experimental evidence, no additional details recorded"
/note="Protein kinase."
Region 720..972
/gene="ERBB2"
/region_name="S_TKc"
/note="Serine/Threonine protein kinases, catalytic domain;
Phosphotransferases. Serine or threonine-specific kinase
subfamily; smart00220"
/db_xref="CDD:47550"
Site 726..734
/gene="ERBB2"
/site_type="np-binding"
/inference="non-experimental evidence, no additional details recorded"
/note="ATP (By similarity)."
Region 742..745
/gene="ERBB2"
/region_name="Beta-strand region"
/experiment="experimental evidence, no additional details recorded"
Region 748..753
/gene="ERBB2"
/region_name="Beta-strand region"
/experiment="experimental evidence, no additional details recorded"
Site 753
/gene="ERBB2"
/site_type="binding"
/inference="non-experimental evidence, no additional details recorded"
/note="ATP (By similarity)."
Region 761..776
/gene="ERBB2"
/region_name="Helical region"
/experiment="experimental evidence, no additional details recorded"
Site order(783,798..805,849..850,862..864)

/gene="ERBB2"
/site_type="other"
/note="ATP binding pocket"
/db_xref="CDD:29154"
Region
785..799
/gene="ERBB2"
/region_name="Beta-strand region"
/experiment="experimental evidence, no additional details recorded"
Region
806..812
/gene="ERBB2"
/region_name="Helical region"
/experiment="experimental evidence, no additional details recorded"
Site
order(807,845,849,882..886)
/gene="ERBB2"
/site_type="other"
/note="peptide substrate binding pocket"
/db_xref="CDD:29154"
Region
814..816
/gene="ERBB2"
/region_name="Helical region"
/experiment="experimental evidence, no additional details recorded"
Region
819..838
/gene="ERBB2"
/region_name="Helical region"
/experiment="experimental evidence, no additional details recorded"
Site
843..852
/gene="ERBB2"
/site_type="other"
/note="catalytic loop"
/db_xref="CDD:29154"
Site
845
/gene="ERBB2"
/site_type="active"
/inference="non-experimental evidence, no additional details recorded"
/note="Proton acceptor (By similarity)."
Region
848..850
/gene="ERBB2"
/region_name="Helical region"
/experiment="experimental evidence, no additional details recorded"
Region
851..855
/gene="ERBB2"
/region_name="Beta-strand region"
/experiment="experimental evidence, no additional details recorded"
Region
858..861
/gene="ERBB2"
/region_name="Beta-strand region"
/experiment="experimental evidence, no additional details recorded"
Site
order(863..868,875..879,882..892)
/gene="ERBB2"
/site_type="other"
/note="activation loop"
/db_xref="CDD:29154"
Region
886..888
/gene="ERBB2"
/region_name="Helical region"
/experiment="experimental evidence, no additional details recorded"

recorded"
Region 891..896
/gene="ERBB2"
/region_name="Helical region"
/experiment="experimental evidence, no additional details
recorded"
Region 901..916
/gene="ERBB2"
/region_name="Helical region"
/experiment="experimental evidence, no additional details
recorded"
Region 924..926
/gene="ERBB2"
/region_name="Beta-strand region"
/experiment="experimental evidence, no additional details
recorded"
Region 928..930
/gene="ERBB2"
/region_name="Hydrogen bonded turn"
/experiment="experimental evidence, no additional details
recorded"
Region 931..937
/gene="ERBB2"
/region_name="Helical region"
/experiment="experimental evidence, no additional details
recorded"
Region 949..958
/gene="ERBB2"
/region_name="Helical region"
/experiment="experimental evidence, no additional details
recorded"
Region 963..965
/gene="ERBB2"
/region_name="Hydrogen bonded turn"
/experiment="experimental evidence, no additional details
recorded"
Region 969..981
/gene="ERBB2"
/region_name="Helical region"
/experiment="experimental evidence, no additional details
recorded"
Region 983..986
/gene="ERBB2"
/region_name="Helical region"
/experiment="experimental evidence, no additional details
recorded"
Region 1020..1022
/gene="ERBB2"
/region_name="Hydrogen bonded turn"
/experiment="experimental evidence, no additional details
recorded"
Site 1139
/gene="ERBB2"
/site_type="modified"
/inference="non-experimental evidence, no additional
details recorded"
/note="Phosphotyrosine; by autocatalysis (By similarity)."
Region 1170
/gene="ERBB2"
/region_name="Variant"
/experiment="experimental evidence, no additional details
recorded"
/note="P -> A. /FTId=VAR_016318."
Region 1195..1197

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/gene="ERBB2"
/region_name="Region of interest in the sequence"
/inference="non-experimental evidence, no additional
details recorded"
/note="Interaction with PIK3C2B (Probable)."
1196
/gene="ERBB2"
/site_type="modified"
/inference="non-experimental evidence, no additional
details recorded"
/note="Phosphotyrosine (Potential)."
Site 1248
/gene="ERBB2"
/site_type="modified"
/inference="non-experimental evidence, no additional
details recorded"
/note="Phosphotyrosine; by autocatalysis (By similarity)."
Site
ORIGIN
1 melaalcrwglallalppgaa astgvctgtd mklrlpaspe thldmlrhly ggcqvvggnl
61 eltylptnas lsflqldiqev qgyvliahnq vrqvpqlrly ivrqtqlfed nyalavldng
121 dplnntptvt gaspgglrel qlrsleikl ggyqlqrnpq lcyqdtlwk difhknqnla
181 ltltdnrsr achcpccpmch gsrcwgesse dcgsllrtvc aggcarckgp lptdccheqc
241 aagctggkhs dclaclhfnh sgicelhcpa ltynttdtfe smpnpegrty fgascvtacp
301 ynylstdvgs ct1vcplhng evtaedgtqr cekcskpccar vcyqlgmehl revravtsan
361 iqefagckki fgsllafipee fdgdpasnta plpgdqlqvft etleelitygl yisawpdslp
421 dlsvfqnlqv irgrilhng ysltlqlgi swiglrsre lgs glalihh nthlcfvhtv
481 pwdqlfrnph gailhtanrp edecvgegla chqlcarghc wggptgcvn csgflrgqec
541 veecrvlggl preyvnarhc lpcpccpqg ngsvtcfge adqcvacahy kdppfcvarc
601 psgvkpdlsy mpiwkfpdee gacqpcpinc thscvdlddk gcpaeqrasp ltsiisavvg
661 illvvvlgvv fgilikrrqq kirkytmrrl lgetelvepl tpsgampnqa qmrilketel
721 rkvkvlgsga fgtvkgiwi pdgenvkipw aikvlrents pkankeilde avymagvgsp
781 yvsrligicl tstvqlvtql mpygclldhv renrgrlgsq dlnnwcmqia kgmsyledrv
841 lvhrlaarn vlvkspnhvk itdfglarll dideteyhad ggkvpiwkma lesilrrfft
901 hqsdvwsygv twwelmtfga kpydgpipare ipdllekger lppgpiictid vymimvkwm
961 idsecprfr elvsefsrma rdpgqrftvqg nedlgpaspl dstfyrsllle dddmgdlvd
1021 eeylvpqggf fcfdpapagag gmwvhhrhrss strsgggdtl lglepseeea prsplapseg
1081 agsdvfdgdl gmgaaaklgq lpthdpsplq ryseadptvpl psetdgyvap ltcspgpeyv
1141 nqpdvprqpp spregplpaa rpagatlerp tlspgkngv vkdvfafgga venpeytlpq
1201 ggaapghpp pafspafdnly ywdqdpert gappstfkgt ptaenpeyig ldvpv
//
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